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Health and Environmental Effects Profile for Pendimethalin

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HEALTH AND ENVIRONMENTAL EFFECTS PROFILE FOR PENDIMETHALIN

ENVIRONMENTAL CRITERIA AND ASSESSMENT OFFICE
OFFICE OF HEALTH AND ENVIRONMENTAL ASSESSMENT
OFFICE OF RESEARCH AND DEVELOPMENT
U.S. ENVIRONMENTAL PROTECTION AGENCY
CINCINNATI, OH 45268

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16. ABSTRACT

The Health and Environmental Effects Profile for Pendimethalin was prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Solid Waste to support listings of hazardous constituents of a wide range of waste streams under Section 3001 of the Resource Conservation and Recovery Act (RCRA). Both published literature and information obtained from Agency program office files were evaluated as they pertained to potential human health, aquatic life and environmental effects of hazardous waste constituents.

Quantitative estimates have been presented provided sufficient data are available. Pendimethalin has been determined to be a systemic toxicant. An Acceptable Daily Intake (ADI), defined as the amount of a chemical to which humans can be exposed on a daily basis over an extended period of time (usually a lifetime) without suffering a deleterious effect, for Pendimethalin is 5×10^{-2} (mg/kg bw/day) for oral exposure.

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PREFACE

Health and Environmental Effects Profiles (HEEPs) are prepared for the Office of Solid Waste by the Office of Health and Environmental Assessment. The HEEPs are intended to support listings of hazardous constituents of a wide range of waste streams under Section 3001 of the Resource Conservation and Recovery Act (RCRA). Both published literature and information obtained from Agency program office files are evaluated as they pertain to potential human health, aquatic life and environmental effects of hazardous waste constituents. The literature searched and the dates of the searches are included in the section titled "Appendix: Literature Searched."

Quantitative estimates are presented provided sufficient data are available. For systemic toxicants, these include, Acceptable Daily Intakes (ADIs) for chronic exposures. An ADI is defined as the amount of a chemical to which humans can be exposed on a daily basis over an extended period of time (usually a lifetime) without suffering a deleterious effect. In the case of suspected carcinogens, ADIs are not estimated in this document series. Instead, a carcinogenic potency factor or q_1^* is provided. These potency estimates are derived for both oral and inhalation exposures where possible. In addition, unit risk estimates for air and drinking water are presented based on inhalation and oral data, respectively.

The first draft of this document was prepared by Syracuse Research Corporation under EPA Contract No. 68-03-3228. The document was subsequently revised after reviews by staff within the Office of Health and Environmental Assessment: Carcinogen Assessment Group, Reproductive Effects Assessment Group, Exposure Assessment Group, and the Environmental Criteria and Assessment Office in Cincinnati.

The HEEPs will become part of the EPA RCRA docket.

ACKNOWLEDGEMENTS

The initial draft of this report was prepared by Syracuse Research Corporation under Contract No. 68-03-3228 for U.S. EPA's Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH. Dr. Christopher DeRosa was the Technical Project Monitor and Helen Ball was the Project Officer. The final documents in this series were prepared for the Office of Solid Waste, Washington, DC.

Scientists from the following U.S. EPA offices provided review comments for this document series:

Environmental Criteria and Assessment Office, Cincinnati, OH
Carcinogen Assessment Group
Exposure Assessment Group
Reproductive Effects Assessment Group

Editorial review for the document series was provided by:
Judith Olsen and Erma Durden
Environmental Criteria and Assessment Office, Cincinnati, OH

Technical support services for this document series were provided by:
Bette Zwayer, Pat Daunt, Karen Mann, and Jacky Bohanon
Environmental Criteria and Assessment Office, Cincinnati, OH.

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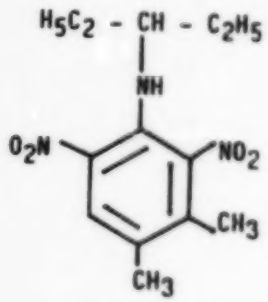
LIST OF ABBREVIATIONS

ADI	Acceptable daily intake
BCF	Bioconcentration factor
LD_{50}	Dose lethal to 50% of recipients
NOEL	No-observed-effect level
ppb	Parts per billion
ppm	Parts per million
UV	Ultraviolet

1. INTRODUCTION

1.1. STRUCTURE AND CAS NUMBER

Pendimethalin is the common name for N-(1-ethylpropyl)-3,4-dimethyl-2,6-dinitrobenzeneamine. Pendimethalin is also known by the product names Prowl, Stomp, Herbadox, Pay-off, Penoxalin and Tendimethalin (NIOSH, 1983). The structure of pendimethalin is given below:



The molecular formula of pendimethalin is $C_{13}H_{19}N_3O_4$ and the molecular weight is 281.35. The Chemical Abstracts Services (CAS) Registry Number for pendimethalin is 40487-42-1.

1.2. PHYSICAL AND CHEMICAL PROPERTIES

Pendimethalin is a crystalline, orange-yellow solid at room temperature with a faint nutty odor (WSSA, 1979). Some of its physical and chemical properties are given below (WSSA, 1979):

Melting point:	54-58°C
Boiling point:	330°C
Vapor pressure:	3.0×10^{-5} mm Hg at 25°C
Water solubility:	0.5 ppm at 23°C
Density:	1.19 at 25°C

1.3. PRODUCTION DATA

Pendimethalin was produced in 1982 by American Cyanamid, Hannibal, MO, and Bafars Nobel, Muskegon, MI (SRI, 1983). It is produced by reacting

2,6-dinitro-3,4-dimethylchlorobenzene with N(1-ethylpropyl) amine (Ayers et al., 1976). No data regarding the production volumes of pendimethalin could be located in the available literature.

1.4. USE DATA

Pendimethalin is a dinitroaniline herbicide applied pre-emergent or pre-plant for controlling annual grasses and broadleaf weeds on a variety of crops. The compound is provided as an emulsifiable concentrate or a granular formulation (WSSA, 1979).

2. ENVIRONMENTAL FATE AND TRANSPORT PROCESSES

Pendimethalin may enter the atmosphere from spray drift or volatilization from treated soil. Parochetti et al. (1976) reported a 2-4% loss of pendimethalin in 3 hours from treated (1.68 kg/ha) sand, clay loam and silt loam in laboratory experiments conducted at various temperatures and soil moisture contents. Oliver (1979) reported vapor losses for pendimethalin of 10 and 1%, 28 days after surface application (0.6 kg/ha) and soil incorporation (1.2 kg/ha) in Matapeake loam, respectively. The experiments were conducted in a volatilization chamber at 70% field moisture capacity, at 22°C, and with an air speed of 11 cm/second. Savage (1978) observed minimal volatilization loss of pendimethalin from sandy loam in greenhouse experiments. The herbicide was incorporated into soil (at 0.5 ppm) at various moisture contents and placed into covered petri dishes; released vapor was collected and analyzed. Moisture content was observed to have little effect on the rate of volatilization, as <0.5 µg pendimethalin/150 gm soil was lost after 8 days at 23°C.

Pendimethalin is subject to losses from photodecomposition (WSSA, 1979); however, no information regarding the vapor phase photodecomposition of the compound is available. Savage and Jordan (1980) observed greater dissipation of surface applied pendimethalin in sunlight and rain soaked field plots as compared to plots in shaded areas. Pendimethalin was applied to sandy loam soil (0.56 kg/ha), and various plots were shaded and exposed to simulated rainfall on day 2 and 6 or day 1 and 3 after application. Approximately 80 or 95% of the applied herbicide was present in the soil 7 days after application in the plots receiving shade and rainfall on days 2 and 6 or days 1 and 3, respectively. Sunlit plots receiving rainfall on days 1 and 3 contained 20-30% of the original herbicide 7 days after application.

Sunlit plots receiving rainfall on days 2 and 6 contained ~50% of the original herbicide 7 days after application. Plots exposed to sunlight alone contained 40-80% of the original herbicide 7 days after application. Parochetti and Dec (1978) studied the photodecomposition of ^{14}C-pendimethalin applied to soil thin layer plates and exposed to sunlight. When compared with treated plates left in the dark, ~9.9% of the herbicide applied (1 kg/ha) to clay loam had photodecomposed in 7 days. In a laboratory experiment, Kennedy and Talbert (1977) measured the percentage of applied pendimethalin (1 kg/ha) that was lost after 24 hours of UV light irradiation (peak energy at 310 nm). Irradiated dry silt loam thin layers kept at 5 and 45°C lost 6 and 26% of the applied herbicide, respectively. A similarly treated thin layer kept at 45°C in the dark lost 12% of the applied herbicide. Treated soils containing 1, 14, 26 and 33% moisture (by weight) lost 9, 17, 24 and 16% of the applied herbicide, respectively.

Several investigators have reported on the fate and persistence of pendimethalin in soil. The dissipation of the compound from the soil depends upon many factors including temperature, moisture content, soil organic matter content and method of application. Nelson et al. (1983) examined the metabolism and soil binding of pendimethalin in samples of sandy loam soil. Soil samples treated with ^{14}C-pendimethalin (1 ppm) and incubated for 0, 1, 2, 4 and 6 months contained 89, 81, 67, 63 and 66% of the parent compound, respectively. Soil bound residues accounted for 11, 11, 15 and 12% of the applied radioactivity after 1, 2, 4 and 6 months, respectively. Less than 1% of the applied radioactivity was evolved as $^{14}CO_2$. Microbial degradation of the herbicide in the soil presumably occurred, because propylene oxide sterilized soil degraded 31% less pendimethalin in 6-month incubations than non-sterile soil. Sterilized soil contained ~50% less

bound radioactivity in 6-month incubations than non-sterile soil. Smith et al. (1979) reported the degradation of pendimethalin in loam soil under anaerobic conditions. Soil (2 kg), 2 ℓ of distilled water and pendimethalin (10 ppm including a ^{14}C tracer) were added to a nitrogen-blanketed glass chamber, and incubated in the dark for 4 and 13 days. Of the recovered radioactivity, 16 and 9.5% was in the form of 1-(1-ethylpropyl)-5,6-dimethyl-7-nitrobenzimidazole after the 4-day and 13-day incubations, respectively. The remainder of the recovered radioactivity was in the form of the parent compound.

Savage (1978) reported that the persistence of pendimethalin in samples of clay soil was greatly affected by soil moisture content, and unaffected by soil sterilization. The half-life of the compound in flooded and moist clay soil under greenhouse conditions was 99 and 37 days, respectively. No significant difference ($p=0.05$) in the dissipation rate of pendimethalin was observed between autoclaved and non-autoclaved clay soil.

Kennedy and Talbert (1977) investigated the effects of delaying the incorporation of pendimethalin for 0, 1, 3 and 7 days on its persistence in field experiments. The herbicide was applied at 0.56 kg/ha to silt loam soil plots, and was incorporated to a depth of 5 cm at the stated times. Gas-liquid chromatographic analysis showed that herbicide losses increased dramatically when incorporation was delayed for $\geq$3 days. The percent of applied herbicide remaining in the soil after delayed incorporation of 1, 3 and 7 days was 88, 62 and 31%, respectively.

The fate of pendimethalin in the aquatic environment is not known. Its low leachability may prevent it from entering groundwater (Schwartz and Alley, 1978). Isensee and Dubey (1983) simulated the fate of the herbicide in a model aquatic ecosystem. Four-hundred-gram quantities of silt loam

soil were treated with ^{14}C-pendimethalin (1 and 10 ppm) and placed in 20 ℓ glass tanks with 16 ℓ of water, mosquito fish, snails, algae and daphnids. Water, soil and tissue samples were taken at various intervals and assayed for radioactivity. A maximum level of radioactivity in water was observed after 13 days, which accounted for 11-13% of the amount applied. Most of the radioactivity measured in water was in the form of polar metabolites, 54% on day 2 increasing to ~90% on days 9-30. The total biomass of all organisms accounted for ~1% of the radioactivity added to the system. In snails, 50% of the radioactivity measured was in the form of the parent compound on day 1; this decreased to <1% by day 15. In fish, the parent compound accounted for 76% of the radioactivity measured on day 1; this decreased to 22% by day 30. After 30 days of exposure to 1.0 ppm pendimethalin, algae, snails, daphnids and fish contained 376, 219, 76 and 26 ppb, respectively. After 30 days of exposure to 10 ppm pendimethalin, algae, snails, daphnids and fish contained 4479, 3616, 525 and 567 ppb, respectively.

3. EXPOSURE

No monitoring data for pendimethalin were contained in STORET. According to the U.S. EPA [45(193) FR 65210] residues of pendimethalin or its metabolites are not likely to occur in eggs, milk, meat, fat or meat by-products when the compound is used as recommended.

According to the U.S. EPA [46(71) FR 21771], pendimethalin may contain carcinogenic nitrosoamine contaminants. Data submitted to the U.S. EPA indicate that the level of this contaminant in pendimethalin is <135 ppm.

Occupational exposure to pendimethalin may occur in pesticide applicators and other farm workers, although no pertinent data regarding the levels of exposure were located in the available literature.

4. PHARMACOKINETICS

Pertinent data regarding the absorption, distribution, metabolism and excretion of pendimethalin in mammals could not be located in the available literature.

5. EFFECTS

5.1. CARCINOGENICITY

The U.S. EPA [46(71) FR 21770-2] has evaluated chronic pendimethalin feeding studies in rats and mice wherein no oncogenic effects were observed at a dietary level of 500 ppm. No experimental details were available.

Pendimethalin may contain carcinogenic nitrosamine contaminants. The U.S. EPA's toxicologists have calculated that if the contaminant is not in excess of 135 ppm, then the upper level of risk would not exceed 1×10^{-6} [46(71) FR 21770-2].

5.2. MUTAGENICITY

Eisenbeis et al. (1981) reported the absence of reverse mutation in a Salmonella typhimurium spot test in the presence of pendimethalin alone or in combination with Banvel, Paraquat, Bladex and Atrazine with or without rat liver S-9 activation. The report states that the test was conducted at full strength and at recommended field concentrations. These figures were not given, but referenced the Illinois Agronomy Handbook.

The U.S. EPA [46(71) FR 21770-2] has evaluated a dominant lethal study with no effects at 2500 ppm, a negative Ames assay (<1000 ug/plate), and a negative host-mediated assay with mice (<16.6 mg/mouse). No experimental details were provided. The limited information preclude any conclusion on the mutagenicity of pendimethalin.

5.3. TERATOGENICITY

The U.S. EPA [46(71) FR 21770-2] has evaluated a teratology study in rats wherein pendimethalin exhibited no teratogenic or fetotoxic effects at doses up to 500 mg/kg/day.

5.4. OTHER REPRODUCTIVE EFFECTS

The U.S. EPA [46(71) FR 21770-2] has evaluated a 3-generation rat reproduction study wherein a NOEL at 500 ppm was observed. No experimental details were provided.

5.5. CHRONIC AND SUBCHRONIC TOXICITY

The U.S. EPA [46(71) FR 21770-2] has evaluated a 90-day pendimethalin feeding study in rats wherein a NOEL of 500 ppm was observed, a 90-day feeding study in dogs wherein a NOEL of 62.5 mg/kg/day was observed, and a 2-year chronic feeding study in rats wherein no systemic effects were observed at 100 ppm; a 2-year feeding study in dogs was under review. These studies were unavailable and no experimental details were provided.

5.6. OTHER RELEVANT INFORMATION

NIOSH (1983) reports an LD_{50} for oral administration to rats and mice of 1250 mg/kg and 1620 mg/kg, respectively.

The U.S. EPA [46(71) FR 21770-2] has evaluated a 21-day dermal study wherein rabbits had a NOEL of 1 g/kg/day, a negative cataractogenic study (3000 ppm), and a study providing a NOEL in male mammary glands at 5000 ppm. No experimental details were provided.

6. AQUATIC TOXICITY

There are relatively few data on the toxicity of pendimethalin on aquatic organisms. Calton and Burnett (1981) reported that pendimethalin, administered at 10 mg/ℓ, was lethal to white perch, Morone americana (exposure not specified, but possibly 16 hours). Pendimethalin at this level did not affect the pulsation or swimming behavior of the jellyfish, Chrysaora quinquecirrha.

The distribution of pendimethalin residues in an aquatic model ecosystem and its bioaccumulation in several aquatic organisms were studied by Isensee and Dubey (1983). Radiolabeled pendimethalin was applied to a soil sample (Matapeake silt loam) at 1.0 and 10.0 mg/kg soil and placed in aquaria. Mosquito fish, Gambusia affinis, snails, Helisoma sp., daphnids, Daphnia magna, and algae, Oedogonium cardiacum, were added to the aquaria. Soil retention was from 81.5-85.4% of the applied pendimethalin. After 13 days only 10.8-12.6% of the applied radioactivity was detected in the water, which was determined to be a polar metabolite of pendimethalin. Uptake of pendimethalin and its metabolites was noted in all species of aquatic organisms. BCFs ranged from 190 for algae to 312 in the mosquito fish (Isensee and Dubey, 1983).

7. EXISTING GUIDELINES AND STANDARDS

7.1. HUMAN

Tolerances for pendimethalin residues on corn, cottonseed, soybeans, potatoes and sorghum have been established by the U.S. EPA at 0.1 ppm [45(193) FR 65209].

The U.S. EPA [46(71) FR 21770-2] has established an ADI for pendimethalin of 0.05 mg/kg/day based on a NOEL of 100 ppm from a 2-year feeding study in the rat, and using an uncertainty factor of 100.

7.2. AQUATIC

Guidelines and standards for the protection of aquatic organisms from the toxic effects of pendimethalin could not be located in the available literature.

8. RISK ASSESSMENT

Insufficient published experimental data are available to evaluate the carcinogenicity of pendimethalin or to derive an ADI for this compound. The U.S. EPA, based on unpublished studies, has calculated an ADI of 0.05 mg/kg/day (see Sections 5.5. and 7.1.) [46(71) FR 21770-2].

In unpublished chronic feeding studies evaluated by the U.S. EPA, no carcinogenic effects were observed in rats or mice at a dietary level of 500 ppm pendimethalin [46(71) FR 21770-2]. Although this pesticide may contain a nitrosamine contaminant, the U.S. EPA has concluded that the contaminant is not present at levels high enough to pose an unacceptable level of risk (see Section 5.1.) [46(71) FR 21770-2].

Statements concerning available literature in this document refer to published, quotable sources and are in no way meant to imply that confidential data, which this document could not address, are not in existence. These data, which are considered Confidential Business Information (CBI), are available in summary form in a CBI Appendix that can be accessed by individuals with appropriate clearance. Conclusions from the CBI Appendix regarding risk assessment can, however, be presented in this chapter.

The CBI Appendix to this document reviews unpublished subchronic and chronic dietary studies of pendimethalin in rats, dogs and mice, some of which appear to be the studies evaluated by the U.S. EPA as described above. These studies are reviewed in greater detail in the CBI Appendix, and a more conservative ADI of 0.005 mg/kg bw/day or 0.35 mg/day for a 70 kg man is recommended. Because a NOAEL for pendimethalin could not be defined, the ADI was based on a dietary LOAEL of 100 ppm (5 mg/kg bw/day, assuming a rat consumes a daily amount of food equal to 5% of its body weight) for enzyme induction, hypertrophy and fatty infiltration in the livers of rats in a

2-year study and using an uncertainty factor of 1000 (a factor of 10 for extrapolating from rats to humans, 10 for using a LOAEL for ADI derivation and 10 for protection of the most sensitive individuals within human population).

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APPENDIX: LITERATURE SEARCHED

This profile is based on data identified by computerized literature searches of:

CA SEARCH (Files 308, 309, 310, 311, 320)
TOXLINE
MEDLINE
RTECS
SCI SEARCH
OHM TADS
STORET
SRC Environmental Fate Data Bases
SANSS
AQUIRE

These searches were conducted in July and August, 1983. In addition, hand searches were made of Chemical Abstracts (Collective Indices 6 and 7th), and the following secondary sources were reviewed:

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